49. (Previously Added) The method of claim 48, wherein said label is selected from a fluorophore, a chromophore, a luminophore, a ferritin, a heavy metal and a radioactive label.

50. (Currently Amended) The method of claim 49, wherein said ~~enzymatic~~ label is selected from horseradish peroxidases, urease, luciferase and alkaline phosphatase.

REMARKS

A. Regarding the Amendments

Claims 1, 5, 6, 7, 9, 40, 42, 48 and 50 have been amended as set forth in the above Listing of the Claims. Claim 8 has been canceled. As amended, the claims are supported by the specification and the original claims and do not add new matter. The amendments do not require a new search or raise new issues for consideration because they merely address issues already raised by the Examiner or define Applicants' invention more clearly. It is submitted that the amendments place the claims in condition for allowance or in better condition for appeal by reducing the number of issues for consideration on appeal. The amendments were not made earlier in the prosecution because it is maintained that the previously pending claims were allowable.

Specifically, claims 1, 7, 9, 40 and 42 have been amended to remove reference to the "thiol-containing mycothiol component" or derivative thereof, in the claims. Claims 5 and 6 were amended simply to correct the dependency of those claims, as they were dependent upon canceled claim 4. Dependency has been corrected to claim 1. Additionally, claim 9 has been amended, as set forth on page 2 of Exhibit A of Applicants' response filed February 14, 2003. The amendments currently made to claim 9 were originally submitted on page 2 of Exhibit A of that response, however, the added language was mistakenly omitted from the claims on page 3 of the response. The amendments to claims 48 and 50 are made simply to clarify the antecedent basis of those claims.

Since the amendments do not add new matter or require a new search or consideration, and place the claims in condition for allowance or in better condition for appeal, entry of the amendment is respectfully requested. Thus, upon entry of the amendments, claims 1-3, 5-7, 9-11, 40, 42 and 48-50 will be pending.

B. **Rejection Under 35 U.S.C. § 101**

As set forth above, the error in amending claim 9 has been remedied by the present action. As set forth on page 3 of the Response filed February 14, 2003, the new language of the claim was unintentionally omitted. By the entry of the claims, as set forth in the above "Listing of the Claims," the intended language has been added to claim 9. Applicants respectfully submit, that as amended claim 9 is directed to "[a]n isolated antibody...," the amended claim overcomes the grounds for rejection. Accordingly, withdrawal of the rejection of claim 9 as containing non-statutory subject matter under 35 U.S.C. §101 is respectfully requested.

C. **Rejection Under 35 U.S.C. § 112**

Applicants respectfully traverse the rejection of claims 1-3, 5-8 and 48-50 under 35 U.S.C. § 112, first paragraph, for allegedly being non-enabled for a method of detecting a member of the taxa actinomycetes comprising detecting reaction of a thiol-selective reagent with a thiol. The Examiner has acknowledged that Applicants have overcome the originally stated rejection, "that Step b of claim 1 recites that one can detect actinomycetes by detecting the reaction of said reagent **or** said antibody..." (Emphasis in the Office Action mailed May 6, 2003; page 3). However, it is alleged that the specification does not support the scope of the amended claims, namely that the antibody specifically binds to a mycothiol derivative, or a derivative of a thiol-containing mycothiol component. Applicants respectfully disagree.

Initially, it is noted that the language "thiol-containing mycothiol component" has been removed from the claim. Accordingly, this response will address the enablement in the specification for specific binding of an antibody to a mycothiol derivative. Additionally, claim 8 has been cancelled.

Claim 1 recites steps of the method of detecting actinomycetes in a sample. These steps include allowing an antibody to specifically bind a mycothiol derivative. Support for inclusion of this step may be found in the specification at page 17, lines 24-26 and the Examples of the application, where specific binding and conditions for specific binding are discussed. Specifically, the step of allowing the antibody to specifically bind a mycothiol derivative is enabled by the Examples. For example, in Example 4, mycothiol is derivatized with maleimide-BSA (page 39, line 1), in Example 5, mycothiol is derivatized with monobromobimane (page 42, line 2), and in Example 8 mycothiol is derivatized with a thiol selective reagent, such that mycothiol is biotinylated (page 45, line 21). These derivatives of mycothiol are merely exemplary and are not meant to limit the subject matter of the invention. Other methods of derivitization of mycothiol will be well known to those of skill in the art and are within the scope of the claimed invention. In Examples 4 and 8, a derivatized mycothiol is immobilized and detected with an antibody.

The Examiner has alleged that "the specification teaches only one polyclonal antibody that binds to mycothiol and not to its carrier proteins, and also does not bind to very specific derivatives." It is believed that the Examiner is referring specifically to Example 7 and corresponding Figure 4. However, Applicants disagree with the Examiner's statement. Of the thiols tested, GSH, Pant and CoA are not derivatives of mycothiol, but are "typical biological thiols," (as set forth on page 44). These thiols are not mycothiol derivatives, and therefore would not be expected to be recognized by an anti-mycothiol antibody. As expected, the results set forth in Figure 4 show affinity of the antibody for these thiols to be less than the control. Similarly, component parts of mycothiol, Cys, NAcCys, CysGlcN and NAcCysGlcN were tested

with the anti-mycothiol antibody. These thiols are not derivatives of mycothiol, but are component parts of mycothiol. It was found that the antibody had an affinity for NAcCysGlcN, which is mycothiol without the inositol, but the affinity of the antibody for the other three components was below the control level. Even where the antibody had an affinity for NAcCysGlcN, it was only about 4% of that of the antibody for mycothiol. This example therefore sets forth, not that the antibody does not have affinity for derivatives of mycothiol, but that the affinity for mycothiol will not be falsely reported by the presence of other biological thiols or component parts of mycothiol. As set forth above, Examples 4 and 8 show binding to derivatives of mycothiol and Examples 4, 7 and 8 show examples of mycothiol derivatized by BSA, monobromobimane or biotinylation.

As such, one of skill in the art would have been able to practice the present invention utilizing the teachings of the specification, in particular, the Examples section, as the amended claims specify that the antibody specifically binds a mycothiol derivative. Therefore, claims 1-3, 5-7 and 48-50 meet the enablement requirement of 35 U.S.C. §112, first paragraph. Accordingly, removal of the rejection is requested.

Applicants also respectfully traverse the rejection of claims 5, 10, 40 and 42 under 35 U.S.C. § 112, first paragraph, for containing subject matter allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the invention at the time of filing of the Application. In particular, it is alleged in the final Office Action mailed May 6, 2003, that claims 5, 10, 40 and 42 are directed to use of monoclonal antibodies and such antibodies are not specifically taught in the specification.

The Examiner's attention is respectfully drawn to the specification at page 11, the last line through page 12, line 1, which defines the antibodies of the application as either polyclonal or monoclonal. Though the examples may be directed to polyclonal antibodies, the examples are not meant to be limiting, but are exemplary. It is respectfully submitted that one of skill in the

art, at the time of filing of the claimed invention, would have been able to practice the claimed methods utilizing monoclonal antibodies, utilizing the polyclonal examples in combination with the known methods of preparation of monoclonal antibodies. Methods of preparation of monoclonal antibodies were well known in the art at the time of filing of the claimed invention, as set forth on page 12, line 23 to page 13, line 24. As stated in the specification, monoclonal antibodies are made from antigen containing fragments of the protein by methods well known to those skilled in the art (Kohler & Milstein, *Nature* 256:495 (1975); Coligan *et al.*, sections 2.5.1-2.6.7; and Harlow *et al.*, *Antibodies: A Laboratory Manual*, page 726 (Cold Spring Harbor Pub. 1988). As such, it would have been routine for one of skill in the art to prepare antibodies as claimed in the present invention.

Therefore, claims 5, 10, 40 and 42 meet the written description requirement of 35 U.S.C. §112, first paragraph. Accordingly, removal of the rejection is requested.

CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 1-3, 5-7, 9-11, 40, 42 and 48-50 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 677-1456. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: August 6, 2003

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